

Patent claims

1. Thermosensitive polymers containing magnetic and/or metallic colloids, characterized in that they can be produced by inverse suspension polymerization and that they have a physical structure which can be changed by magnetic induction.
2. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 1, characterized in that the polymers consist of poly-N-isopropylacrylamide, poly-N-substituted acrylamides, poly-N-substituted methacrylamides, copolymers of monomers from the group comprising N-isopropylacrylamide, N-substituted acrylamides and N-substituted methacrylamides, or mixtures of the aforementioned polymers or/and copolymers.
3. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 2, characterized in that the polymers contain one or more copolymers or block copolymers which apart from the monomer(s) mentioned contain one or more comonomers preferably selected from the group of monomers containing carboxyl groups, such as acrylic acid, methacrylic acid, or from acrylates, acrylate derivatives, methacrylates, methacrylate derivatives, acrolein, acrylamide, N-substituted acrylamides and vinyl acetate.
4. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 2 or 3, characterized in that the polymers contain one or more copolymers or block copolymers selected from the group comprising polyacrylic acid, polyacrolein, polymethacrylic acid, polyacrylamide, N-substituted polyacrylamides and mixtures of the same.

polymethacrylic acid, polyacrylamide, N-substituted polyacrylamides and mixtures of the same.

5. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 4, characterized in that the polymers are nano-particles or microparticles.
6. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 1, characterized in that the magnetic induction consists of a high-frequency, magnetic alternating field.
7. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 1, characterized in that the change in the physical structure consists of a change to the geometric form of the polymers.
8. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 7, characterized in that the change in the geometric form consists of a return to the original form displayed by the polymers before a change in form caused by heat ("shape-memory-polymer").
9. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 1, characterized in that the change in the physical structure consists of an enlargement or reduction in size of the polymer particles.
10. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 9, characterized in that the magnetic colloids consist of ferromagnetic, superparamagnetic, ferrimagnetic

particles, low-temperature-ferrites or a ferrofluid with a particle size of <1  $\mu\text{m}$ .

11. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 10, characterized in that the low-temperature-ferrites have a Curie temperature in the range 30°C to 100°C.

12. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 11, characterized in that the metallic colloids consist of elements from the groups 8, 9, 10 or 11 (group classification: new suggestion IUPAC 1986).

13. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 12, characterized in that the magnetic and/or metallic colloids are present in the form of a core polymer that surrounds them.

14. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 13, characterized in that the core polymer has a particle size of 50 to 1000 nm.

15. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 13 or 14, characterized in that magnetic and/or metallic colloids encapsulated in the core polymer are present in a disperse colloid form.

16. Thermosensitive polymers in accordance with one of Claims 13 to 15, characterized in that the encapsulating core polymer is from the group chitosan, dextran, starch, polyacrylic acid, polysaccharides, silica gel, silicone derivatives, cellulose, proteins, albumin.

polyacrylic acids, agarose, alginate, polystyrene, polyacrylates, polymethacrylates, polycyanoacrylates, polymethyl methacrylate, polyvinyl alcohol, polyamides, polyesters, polyamino acids, hyaluronic acid, polylactides, polyglycolides, polyacrolein and copolymers of the same.

17. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 16, characterized in that the polymers contain 0.1-30 % by weight of a porogen.
18. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 17, characterized in that the porogen is from the group silica gels, proteins, nucleic acids, polyethylene glycols, polyethylene oxides and polysaccharides.
19. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 18, characterized in that the polymers are cross-linked with a bi- or tri-functional cross-linking agent.
20. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 19, characterized in that the cross-linking agent has a concentration of 0.1% to 10% relative to the overall monomer content.
21. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 20, characterized in that the polymers have reactive groups that bond biomolecules.
22. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 21,

conjugates, oligosaccharides, glycoproteins, lectins, nucleic acids, streptavidin or biotin.

23. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of Claims 1 to 22, characterized in that the polymers contain at least one encapsulated active agent which can be released from the polymer into the environment by exposure to a magnetic field.

24. Thermosensitive polymers containing magnetic and/or metallic colloids in accordance with Claim 23, characterized in that the encapsulated active agents are selected from the group hormones, cytostatic agents, antibodies, antibody derivatives, antibody fragments, cytokines, immunomodulators, antigens, proteins, peptides, lectins, glycoproteins, nucleic acids, antisense-nucleic acids, oligosaccharides, antibiotics or generic agents.

25. Process for the production of thermosensitive polymers in accordance with one of Claims 1 to 24, characterized in that an aqueous monomer solution in which the magnetic and/or metallic colloids are dispersed is suspended through mechanical comminution in an organic phase that is not miscible with water after adding a multifunctional cross-linking agent and a radical initiator and is radically polymerized to nano- or microparticles.

26. Process for the production of thermosensitive polymers in accordance with one of Claims 1 to 24, characterized in that an aqueous monomer solution in which the magnetic and/or metallic colloids are dispersed is suspended through mechanical comminution in an organic phase that is not miscible with water after adding a multifunctional cross-linking agent and is radically polymerized to nano or microparticles during the suspension process through the addition of a radical initiator.

27. Process for the production of thermosensitive polymers in accordance with Claim 25 or 26, characterized in that N-isopropylacrylamide, N-substituted acrylamides, N-substituted methacrylamides or mixtures of the same are used as a monomer.

28. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 to 27, characterized in that 0.05 to 30 % by mol co-monomers are added to the monomer solution.

29. Process for the production of thermosensitive polymers in accordance with Claim 28, characterized in that the co-monomers are acrylate derivatives, methacrylate derivatives, acrylic acid, acrolein, methacrylic acid, acrylamide, vinyl acetate or mixtures of the same.

30. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 to 29, characterized in that ferromagnetic, superparamagnetic or ferrimagnetic substances or low-temperature ferrites or ferrofluids with a particle size of <1 µm are added to the monomer solution.

31. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 to 30, characterized in that the ferromagnetic, superparamagnetic or ferrimagnetic substances or low-temperature ferrites are present as colloids or in a powder form.

32. Process for the production of thermosensitive polymers in accordance with Claim 25 or 26, characterized in that a nano or microparticle core polymer in which the magnetic and/or metallic colloids are dispersively encapsulated is added to the monomer solution.

33. Process for the production of thermosensitive polymers in accordance with Claim 32, characterized in that the core polymer is formed by chitosan, dextran, starch, polyacrylic acid, polysaccharides, silica gel, silicone derivatives, cellulose, proteins, albumin, polyacrylic acid, agarose, alginate, polystyrene, polyacrylates, polymethacrylates, polycyanoacrylates, polymethyl methacrylate, polyvinyl alcohol, polyamino acids, hyaluronic acid, polylactides, polyglycolides, polyacrolein or copolymers of the same.

34. Process for the production of thermosensitive polymers in accordance with Claims 25 or 26, characterized in that solvents used as the organic phase have a polar solubility parameter of  $5-10 \text{ (cal/cm}^3\text{)}^{1/2}$ .

35. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 or 26, characterized in that 0.05 to 15 % by weight of one or more surfactive substances is added to the organic phase.

36. Process for the production of thermosensitive polymers in accordance with Claim 35, characterized in that the surface active substance is from the group alkyl sulphosuccinates, polyoxyethylene aryl ethers, polyoxyethylenes, polyoxyethylene sorbitan esters, polyoxyethylene adducts, polyethylene propylene oxide block copolymers, alkylphenoxy polyethoxy ethanols, fatty alcohol polyethylene glycol ethers, polyglycerol esters, polyoxyethylene alcohols, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene acids and mixtures of the same.

37. Process for the production of thermosensitive polymers in accordance with Claim 25, characterized in that the monomer solution is pre-polymerized before dispersion in the organic phase for 5-120 seconds.

38. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 to 37, characterized in that affinity ligands, peptides, proteins, antibodies, antigens, enzymes, cell receptor antibodies, antibodies against tumor markers, antibodies against tumor antigens, antibody fragments, artificially produced antibodies, modified antibodies, antibody conjugates, oligosaccharides, glycoproteins, lectins, nucleic acid, streptavidin or biotin are bonded to the polymers.

39. Process for the production of thermosensitive polymers in accordance with one of the Claims 25 to 38, characterized in that active agents are encapsulated in the polymers, preferably by adding the active agent(s) to a monomer solution containing magnetic and/or metallic colloids.

40. Process for the production of thermosensitive polymers in accordance with Claim 39, characterized in

that the active agents are selected from the group hormones, cytostatic agents, antibodies, cytokines, immunomodulators, antigens, proteins, peptides, lectins, glycoproteins, nucleic acids, antisense-nucleic acids, oligosaccharides, antibiotics and generic agents.

41. Process for the production of thermosensitive polymers in accordance with one of the Claims 39 or 40, characterized in that 0.1 to 20 % by weight of polyvalent alcohols, polyvinyl alcohols, gelatins or carbohydrates are added to the active agents.

42. Process for the production of thermosensitive polymers in accordance with Claim 41, characterized in that the polyvalent alcohols or carbohydrates are from the group inosite, mannite, sorbite, aldonite, erythrite, sucrose, glycerine, xylite, fructose, glucose, galactose and maltose.

43. Process for the release of active agents from active agent-containing particles, characterized in that particles of thermosensitive polymers according to one of Claims 1 to 24 or particles which have been produced in accordance with a process according to one of Claims 25 to 44 are introduced into a magnetic alternating field, preferably a high-frequency magnetic alternating field, for the purpose of magnetic induction.

44. Process for changing the physical structure of thermosensitive polymers containing magnetic and/or metallic colloids, or for warming or heating such polymers, characterized in that said polymers are introduced into a magnetic alternating field, preferably a high-frequency magnetic alternating field, for the purpose of magnetic induction.

45. The use of thermosensitive polymers containing magnetic and/or metallic colloids in accordance with one of the Claims 1 to 24 or of particles produced in accordance with a process according to one of Claims 25 to 44 as contrast-intensifying media in NMR diagnostics, as carriers for active agents in medical therapy and diagnostics, as controllable carriers for reactants, as media to control microfluid processes, as separation media in column chromatography, as media to adjust and regulate pore sizes in membranes, as media to block blood vessels, as artificial cell carriers, as separation media for nucleic acids, cells, proteins, steroids, viruses or bacteria, in each case by using a magnetic alternating field, preferably a high-frequency magnetic alternating field.